Citation:

Gates PE, Tanaka H, Hiatt WR, Seals DR. Dietary sodium restriction rapidly improves large elastic artery compliance in older adults with systolic hypertension. *Hypertension*. 2004 Jul; 44 (1): 35-41.

PubMed ID: 15173128

Study Design:

Randomized controlled trial

Class:

A - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

To determine the effects of dietary sodium restriction on directly measured carotid artery compliance in middle-aged and older men and women with stage I systolic hypertension (HTN).

Inclusion Criteria:

- 50 years or older
- Stage I HTN
- Not using anti-hypertensive medications
- No overt signs of disease on physical examination and medical history
- Normal blood chemistry
- Negative ECG-monitored exercise test
- Ankle-brachial index ≤0.9
- Absence of plaque on ultrasound interrogation of the carotid and femoral arteries
- Non-smoker for previous two years
- Body Mass Index <35kg/m^2
- Not consuming a low-sodium diet
- Post-menopausal, if female (amenorrheic for at least two years).

Exclusion Criteria:

None.

Description of Study Protocol:

Recruitment

- Not described
- 12 of 71 subjects who responded to recruitment efforts successfully completed screening.

Design

Randomized, double-blind, placebo-controlled, crossover trial.

Dietary Intake/Dietary Assessment Methodology

Three-day dietary records were analyzed at baseline and at the end of each condition of the intervention.

Blinding Used

Primary investigators and subjects were unaware of the order of tablet administration.

Intervention

- Subjects were randomized to four-week periods of reduced and normal sodium intake. Subjects reduced dietary sodium intake and were asked to take a prescribed number of tablets with each meal. For four of the weeks, the tablet was placebo and for the other four weeks, the tablet was slow-release sodium chloride. The number of tablets taken was based on a once-weekly 24-hour urinary sodium excretion analysis in comparison to the average of two samples collected at baseline
- Subjects were given comprehensive dietary education and counseling (at baseline and once per week throughout the intervention period) to reduce sodium intake without changing caloric intake or dietary composition.

Statistical Analysis

- A two-way within subjects ANOVA was conducted to evaluate the effect of condition (low and normal) on time (weeks one and four) on arterial compliance and casual resting blood pressure. The condition x time main effect was tested using Wilks λ. Where a significant main effect was found, paired samples T-tests were conducted to determine differences between specific baseline and intervention weeks
- Bivariate relations were determined using Pearson correlation coefficients
- To determine whether the changes in carotid artery compliance and β-stiffness index at week two of the low-sodium condition were independent of the change in mean arterial pressure, separate bivariate linear regression analyses were performed with mean carotid pressure entered as the predictor variable.

Data Collection Summary:

Timing of Measurements

- Casual blood pressure measurements were made during three weekly visits at baseline and once each week during the intervention period
- Ambulatory blood pressure measurements were made during normal daily activity in 11 subjects for 24 hours
- Dietary analysis using three-day dietary records was conducted at baseline and at the end of each condition of the intervention
- Large elastic artery compliance and β-stiffness index were measured at baseline and weekly during the intervention.

Dependent Variables

- Carotid artery compliance and β-stiffness index were determined using high-resolution B-mode ultrasound and simultaneous estimates of carotid blood pressure using applanation tonometry
- Casual brachial artery blood pressure measurements were made after an overnight fast in the upright seated and supine positions
- Ambulatory blood pressure measurements were made during normal daily activity.

Independent Variables

- Low sodium intervention
- Normal sodium intervention.

Control Variables

None.

Description of Actual Data Sample:

- *Initial N:* 12 (6 men and 6 women)
- *Attrition (final N):* 12
- *Age:* Mean (standard error) for men and women was 63 (1) and 64 (4), respectively
- *Ethnicity:* White
- *Other relevant demographics:* None
- *Anthropometrics:* Mean (standard error) of BMI at baseline was 25.1 (1) kg/m^2
- *Location:* US.

Summary of Results:

Other Findings

- Dietary sodium intake was 135mmol per day at baseline and 57mmol per day during the intervention. The slow-release tablets were effective in maintaining urinary sodium excretion at levels not different from baseline
- Compared with baseline, carotid artery compliance was increased ($P<0.05$) by the end of the first week of low-sodium (over 27%), reached its highest value in week two (over 46%, $P<0.01$), and remained elevated during weeks three and four. The changes in β-stiffness index inversely mirrored these changes in carotid artery compliance
- Compared with baseline supine SBP was reduced by greater than 5mmHg by the end of the first week of the low-sodium condition, attaining its nadir (12mmHg, $P<0.01$) by the end of week two. Supine DBP was reduced by three to 6mmHg below baseline during the low-sodium condition ($P<0.05$)
- Compared with baseline, 24-hour SBP was slightly lower by the end of the first week of the low-sodium condition, reached its nadir by week two (-6mmHg, $P<0.01$), and remained lower during weeks three and four. The 24-hour DBP decreased ($P<0.05$) below baseline values throughout the sodium condition as a result of non-significant decreased in daytime and nighttime levels.

Author Conclusion:

Moderate dietary sodium restriction in middle-aged and older adults with untreated stage I systolic HTN rapidly normalizes systolic blood pressure, which may be mediated by an increase in large elastic artery compliance.

Reviewer Comments:

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions		
1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	Yes
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes

Validity Questions		
1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**	Yes
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	???

3.	**Were study groups comparable?**	N/A
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	N/A
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	N/A
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	N/A
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	N/A
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	N/A
4.1.	Were follow-up methods described and the same for all groups?	N/A
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	N/A
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	N/A
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	Yes
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	Yes
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	Yes
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	N/A
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A

5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	Yes
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	N/A
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	N/A
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	Yes
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	No
7.1.	Were primary and secondary endpoints described and relevant to the question?	No
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	???
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	No
7.6.	Were other factors accounted for (measured) that could affect outcomes?	N/A
7.7.	Were the measurements conducted consistently across groups?	Yes
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**	No
8.1.	Were statistical analyses adequately described and the results reported appropriately?	No
8.2.	Were correct statistical tests used and assumptions of test not violated?	No

8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	N/A
8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	N/A
8.6.	Was clinical significance as well as statistical significance reported?	N/A
8.7.	If negative findings, was a power calculation reported to address type 2 error?	N/A
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**	Yes
9.1.	Is there a discussion of findings?	Yes
9.2.	Are biases and study limitations identified and discussed?	???
10.	**Is bias due to study's funding or sponsorship unlikely?**	Yes
10.1.	Were sources of funding and investigators' affiliations described?	Yes
10.2.	Was the study free from apparent conflict of interest?	Yes